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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/676,248	09/30/2003	Peter K. Rogan	33026	5913

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EXAMINER	
POHNERT, STEVEN C	
ART UNIT	PAPER NUMBER
1634	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/676,248	ROGAN ET AL.	
	Examiner	Art Unit	
	STEVEN C. POHNERT	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 March 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-33,43-52 and 54* is/are pending in the application.

4a) Of the above claim(s) *1-33* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *43-52 and 54* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *30 September 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Sequence compliance

The application fails to comply with CFR 1.821(d), which states:

(d)Where the description or claims of a patent application discuss a sequence that is set forth in the "Sequence Listing" in accordance with paragraph (c) of this section, reference must be made to the sequence by use of the sequence identifier, preceded by "SEQ ID NO:" in the text of the description or claims, even if the sequence is also embedded in the text of the description or claims of the patent application.

For example, table 2 starting on page 34, contains a nucleic acid sequence that are improperly identified by "SEQ ID", not the required "SEQ ID NO:". Further the sequences disclosed in table 2 are different than those in the sequence listing. For example SEQ ID 1 of table 2 identifies a 30 nucleotide sequence, while SEQ ID NO 1 of the sequence listing is 1820 nucleotides in length. Applicant is required to correctly identify sequences by "SEQ ID NO:" and insure that sequences identified by SEQ ID NO are consistent with the sequence listing. If those sequence presented in table 2 are fragments or primers of the full length SEQ ID NO, applicant may identify the sequence relative to the full length SEQ ID NO (i.e. nucleotides 1-30 of SEQ ID NO: 1). The applicant should review the rest of the disclosure for any other nucleic acid or protein sequences and list them in a sequence listing and identify them with a proper SEQ ID NO.

The specification and sequence listing must be amended to bring it into sequence compliance. **For any response to this office action to be fully compliant,**

the response has to bring the application in compliance with sequence rules.

Response to Arguments

The response has amended the specification to recite, "SEQ ID NO" however, 37 CFR 1.821 (d) requires the specification to recite, "SEQ ID NO:." Although the response is not completely compliant with respect to this issue the examiner is examining the application in order to promote compact prosecution.

Claim status

This action is in response to claims filed 3/26/2010 and the arguments filed 7/23/2009..

Claims 1-33 are withdrawn.

Claims 34-42 are canceled.

Claims 43-52 and 54 are under consideration.

Claims 43, 47, 49, and 54 have been amended.

The objection to the specification due to the discrepancies between the table and sequence listing has been withdrawn.

The 102 based on Knight has been withdrawn in view of the amendment to require conventional FISH.

Specification

1. The disclosure is objected to because of the following informalities:

The specification is objected to for the sequence compliance issues disclosed above in the sequence compliance section. Applicant must correctly identify the nucleic acid sequences by "SEQ ID NO:".

Appropriate correction is required.

Response to Arguments

The response has amended the specification to recite, "SEQ ID NO" however, 37 CFR 1.821 (d) requires the specification to recite, "SEQ ID NO:." Although the response is not completely compliant with respect to this issue the examiner is examining the application in order to promote compact prosecution.

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 43, 45-47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Knight et al (Am. J. Human Genetics (2000) volume 67, pages 320-332) in view of Boyle et al (Current Protocols in Molecular biology (1992)3.18.1-3.18.9).

The claims are drawn to a method of detecting cytogenetic abnormalities in an individual comprising screening at least one chromosome by hybridization of a plurality of single probes of known sequences, hybridizing the probes to at least one chromosome and detecting hybridization patterns of the probes, said hybridization patterns indicating cytogenetic abnormalities when present. The claim only requires the detection of cytogenetic abnormalities if present.

With regards to claim 43, Knight et al teaches a method of fluorescence in situ hybridization (FISH) on interphase chromosomes (see page 322, 1st column). Knight et al teaches the probes were labeled and detected. Knight et al teaches the probes and the distance from the telomere (terminal nucleotide) in table 1. Knight teaches the distance from the terminal nucleic acid was as little as 268-296 kb for 6ptel48 and teaches sequencing of the probes (see page 322, 2nd column, 1st paragraph). Knight thus teaches method of detecting cytogenetic abnormalities with a plurality of probes within 600 kb of the terminal nucleotide of the chromosome by screening at least one chromosome by hybridization with probes of known sequences, and detecting cytogenetic abnormalities when present. Knight teaches the probes were synthesized by Nick translation. Nick translation results in probes between 2 and 5 kb in length.

With regards to claim 45, Knight teaches that 60 + probes did not cross hybridize (see tables 1 and 3).

With regards to claim 46, Knight teaches the probes had known sequences as demonstrated by the primers of table 2.

With regards to claim 47, Knight teaches the probes were nick translated. Nick translation results in a plurality of short probes of between 50 bp and 12 kb.

Knight teaches the use of FISH, interphase FISH and Fiber FISH for screening of probes.

Boyle et al teach optimal probe length for non-isotopic in situ hybridization is 100 to 500 nucleotides and this is determined by DNase treatment (3.18.8).

Therefore it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use any of the FISH methods disclosed by Knight to screen for cytogenetic abnormalities and produce nick translated probes of 100 to 500 nucleotides in length. The artisan would be substituting one method of cytogenetic FISH analysis for another. Further the artisan would be motivated to produce probes of 100 to 500 nucleotides in length by nick translation as suggested by Knight as Boyle teaches 100 to 500 nucleotides are optimal for in situ hybridization. The artisan would have a reasonable expectation of success as Knight demonstrates that FISH, interphase FISH and Fiber FISH work and Boyle demonstrates the nick translation optimally produces probes of 100 to 500 nucleotides in length..

Response to Arguments

The response asserts the instant amendment to require conventional FISH has overcome the art of Knight as the response asserts that Knight teaches FiberFISH. These arguments have been thoroughly reviewed but are not considered persuasive as

the specification lacks a limiting definition of "conventional FISH." Thus the broadest reasonable interpretation of "conventional FISH," in the instant case is something other than FiberFISH, thus the teachings of Knight of FISH or interphase FISH render these limitations obvious.

5. Claims 44, 48, 49-52, and 54 are rejected under 35 U.S.C. 103(a) as being unpatentable over Knight et al (A) (Am. J. Human Genetics (2000)volume 67, pages 320-332) and Boyle et al (Current Protocols in Molecular biology (1992)3.18.1-3.18.9) in view of Knight (b) (Journal of Medical Genetics (2000) volume 37, pages 401-409).

The claims are drawn to a method of detecting cytogenetic abnormalities in an individual comprising screening at least one chromosome by hybridization of a plurality of probes of known sequences, hybridizing the probes to at least one chromosome and detecting hybridization patterns of the probes, said hybridization patterns indicating cytogenetic abnormalities when present. The claim only requires the detection of cytogenetic abnormalities if present.

The teachings of Knight (A) and Boyle are set forth above.

However, Knight (B) et al teaches, “Chromosomal rearrangements involving the ends of chromosomes (telomeres) are emerging as an important cause of human genetic diseases. This review describes the development of first and second generation sets of telomere specific clones, together with advances in fluorescence in situ hybridization (FISH) technology, which have made the prospect of screening for telomeric rearrangements a realistic goal. Initial FISH studies using the telomere specific clones indicate that they will be a valuable diagnostic tool for the investigation of

mental retardation, the characterization of known abnormalities detected by conventional cytogenetic analysis, spontaneous recurrent miscarriages, infertility, hematological malignancies, and preimplantation diagnosis, as well as other fields of clinical interest. In addition, they may help investigate telomere structure and function and can be used in the identification of dosage sensitive genes involved in human genetic disease.(see abstract). Knight et al further teaches, "The results suggested that at least 6% of idiopathic mental retardation might be explained by submicroscopic rearrangements involving telomeres. If true, then subtelomeric rearrangements could be the second most common cause of mental retardation after Down's syndrome. Therefore, it was important to extend these studies to include all possible telomeres and a larger sample set." Knight (b) further teaches, "The first method, the use of DNA polymorphisms, requires DNA samples from the child and both parents. When both parents are heterozygous and share no alleles, a rearrangement in the child can be inferred from the presence of only a single allele (a deletion) or the presence of three alleles (a trisomy). This technique has the advantage of being able to detect isodisomy (the inheritance of two chromosome homologues from one parent), but it is limited by the degree of polymorphism of the marker and by the need to have access to samples from both parents. Indeed, marker informativity must be very high for this technique to be efficient."

Therefore it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use the method of cytogenetic analysis and probes taught by Knight (A) and Boyle to associate specific hybridization patterns with

clinical abnormalities as taught by Knight (b), because Knight (B) teaches it would allow for better understanding of the clinical abnormalities. Knight (b) specifically teaches the such methods can be used to better understand the causes of idiopathic mental retardation and/or cancers. It would have further been prima facie obvious to compare the sequences to standard genetic maps as Knight (B) teaches comparison of hybridization of children to parents (standard genetic maps). The artisan would have a reasonable expectation of success as Knight(A) and Knight (B) both teach method of detecting polymorphisms by FISH.

Response to Arguments

The response asserts that the combination of Knight (A) and Knight (B) would result in the use of Fiber FISH. This argument has been thoroughly reviewed but is not considered persuasive as Knight (A) teaches the use of FISH and interphase FISH which are broadly encompassed by the claimed "conventional FISH," as the claims lack a limiting definition.

Summary

No claims are allowed over prior art cited.

Conclusions

6. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to STEVEN C. POHNERT whose telephone number is (571)272-3803. The examiner can normally be reached on Monday-Friday 6:30-4:00, every second Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave Nguyen can be reached on 571-272-0731. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Steven C Pohnert/
Primary Examiner, Art Unit 1634